Remarks

Claims 24 and 28-32 were previously pending in the subject application. By this Amendment, applicants have amended claims 29 and 32 and have added new claims 33-38. No new matter has been added by this Amendment.

The claims added to this application are supported throughout the Specification and in particular in the examples where it is disclosed that isolated plant microspores are treated with mixed duplex oligonucleotides resulting in a genomic mutation.

New Claims 33-36

Newly added Claims 33-38 contain the limitation that the microspores must be "isolated" from a plant. This limitation is analogous to the "isolated" limitation commonly seen in claims to polynucleotides, DNA, proteins and bacterial strains where the limitation distinguishes the subject matter of the claims from products found in nature. The newly added claims are therefore distinguishable from any microspore found in nature and a rejection under 35 USC ∋101 would be unwarranted.

Written Description (Claims 24 and 28-32)

The present Specification makes its perfectly clear to one of ordinary skill in the art how to practice the presently claimed invention. A mixed duplex oligonucleotide (MDON) is prepared that has homologous and heterologous regions to the targeted gene. The heterologous region is where the mutation (addition, deletion, replacement) occurs. Limiting the Applicants to only the MDONs specified in the Specification would akin to depriving the Applicants of the value of their invention. As stated before, the Kmiec '350 and '181 patents have claims and specification language of similar scope. Withdrawal of the written description rejection to Claims 24 and 28-32 is respectfully requested.

Enablement (Claims 24 and 28-32)

All of the presently pending claims are fully enabled under the requirements of 35 USC ∋112. Gene repair, in and of itself, was known in the art at the time of the present priority date. See Kmiec '350 and Kmiec '181 both of record in this application which describe and broadly claim gene repair

methods. The scope of the present claims is similar to the scope of the Kmiec '350 and Kmiec '181 patent claims in that they do not specify a specific gene or a specific oligonucleotide. The present claims, however, have limitations that distinguish them as being patentably distinct from both Kmiec patents. US Patents are presumed to be valid and the correlation between the scope of the claims and the specifications of the '350 and '181 issued patents is very analogous to the scope of the present claims and the present Specification. Withdrawal of the rejection to Claims 24 and 28-32 is respectfully requested.

Novelty (Claims 30-32)

Claims 30-32 are not anticipated by the Hawkes et al reference already on the record. Hawkes et al **DO NOT** teach the use of gene repair in micropsores. Rather, Hawkes et al teach the use of gene repair with pollen. Pollen and microspores are distinct tissues. The only relationship between pollen and microspore is that pollen cells are derived from microspore cells. Pollen cells are **incapable** of giving rise to microspores. Microspores that preferentially go on to form microspore-derived embryos (MDEs) do not form a bi-nucleate stage or a tube cell nucleus like pollen cells do and hence are **incapable** of giving rise to pollen cells. Nor are MDEs able to fertilize the female reproductive structure of the plant like pollen can. MDEs are produced directly from uni-nucleate microspores that are not permitted to develop into pollen. For these reasons Hawkes et al is incapable of supporting a novelty rejection under 35 USC ∋102 nor an obvious rejection under 35 USC ∋103. Withdrawal of the 102 rejection is respectfully requested.

Obviousness (Claims 24 and 28-32)

All of the pending claims are non-obvious in view of Kmiec '181 in view of Fennell et al both already of record. The Fennell et al reference teaches the **transformation** of microspores, which is a technique known in the art. The problem is that the presently claimed gene repair (resulting in mutations to genes *in vivo*) can be considered in many respects to be the antithesis of plant transformation. Plant transformation involves the insertion of genes into plants. Gene repair only swaps out, adds or deletes single nucleotides in a native gene. Plant transformation employs large polynucleotide vectors while gene repair uses small oligonucleotides that are chemically

different from the large vectors used in transformation and which are incapable of being incorporated into the host DNA, the most important characteristic of a transformation vector. Plant transformation is a random event. Gene repair is targeted to a specific nucleotide in the plant genome where a change is made to the native gene. For all of the above reasons it is clear that the present claims are not obvious over art that teaches transformation of microspores. Nothing in the microspore transformation methodology would indicate predictability or likelihood of success of the presently claimed microspore gene repair process. Withdrawal of the 103 rejection to Claims 24 and 28-32 is respectfully requested.

In view of the foregoing remarks and the amendments above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicant also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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